

U.S. Application No. 09/147,693
Reply to Office Action dated June 15, 2004
Amendment dated September 15, 2004

REMARKS

Claims 38-45, 49-62, 69, 70, 77 and 78 were pending in the present application. By this Amendment, Applicants have amended claims 38, 50, 69, 70, 77, and 78 to address the Examiner's concerns. Support for the claim amendments can be found in the specification and claims as originally filed. The present Amendment introduces no new matter, and thus, its entry is requested.

The June 15, 2004 Office Action

Claim Rejections - 35 USC § 112, first paragraph

The Examiner rejected claims 69-70, and 77-78 are rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement. According to the Examiner, the claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claim invention. The Examiner stated that this ground of rejection would mostly likely be applicable to claims 50-62 if they were not dependent upon cancelled claim 46.

The Examiner stated that the rejected claims are each drawn to a bacterial cell comprising a bacterial expression control sequence comprising an operator sequence from a lambdoid phage where the operator sequence has a different thermostability compared to a wild-type operator sequence with regard to binding of a repressor wherein the different thermostability results in

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repression of expression of a gene that is operatively linked to the operator sequence until a temperature is reached that is 3 to 10° C higher than the temperature at which the wildtype sequence is capable of repressing expression of the operatively linked gene. According to the Examiner, each of the claims embraces a broad genus of operator sequences obtainable from literally any “lambdoid” phage that must meet the very specific functional limitation of binding a repressor (of any type) at temperatures 3 to 10° C higher than the temperature at which the wildtype operator sequence binds the same repressor.

The Examiner acknowledged that the instant specification is enabling for screening for such mutant operator sequences, but asserted that it only provides description of a single example of a mutated operator sequence that meets the functional limitations of the claims (i.e. SEQ ID NO:2). The Examiner stated that no other sequence is given in the originally filed specification of any other mutated operator sequence that meets the functional limitations of the claims. Nor, according to the Examiner, is any description provided of the domains within the broadly claimed class of lambdoid operator sequences that are well conserved among different lambda species and mutation of which would necessarily provide a mutant operator sequence that meets the functional limitations of the claims. Thus, in the Examiner’s opinion, the instant specification does not provide a structural/functional basis for the skilled artisan to envision the changes to a given lambdoid operator sequence that will satisfy the functional limitations of the claims.

The Examiner noted that the approach taught by applicants for identifying mutated

lambdoid operator sequences that meet the functional limitations of the claims appears to be novel in the art. The Examiner asserted, however, that the prior art does not offset the supposed deficiencies of the instant specification with regard to providing a structural/functional basis for the skilled artisan to envision a sufficient number of specific operator sequences that meet the functional limitations of the rejected claims so as to describe the broadly claimed genus of such operator sequences.

The Examiner's position is therefore that given that the rejected claims encompass a broad genus of operator sequences that must meet very specific functional limitations, and given that the instant specification and prior art do not provide a structural/functional basis for the skilled artisan to envision a sufficient number of specific embodiments of such operator sequences to describe the broadly claimed genus of operator sequences, the skilled artisan would not have been able to envision a sufficient number of mutated sequences that meet the thermostability requirements of the claims to describe the broadly claimed genus of such sequences. Therefore, in the Examiner's view, the skilled artisan would have reasonably concluded that the Applicants were not in possession of the claimed invention at the time of filing the application.

In response, without conceding the correctness of the Examiner's position, but to expedite allowance of the subject application, Applicants have amended claims 50, 69, and 70 to refer to OR or OL operator sequences from bacteriophage lambda, rather than "lambdoid" phages. Applicants believe this amendment fully addresses the Examiner's concerns over the breadth of the term "lambdoid." Applicants also note that the specification discloses the corresponding

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lambda operator wild type sequences. Claim 50 has been rewritten in independent form to no longer depend from canceled claim 46. Applicants believe that the above claim amendments fully overcome the rejections under 35 U.S.C. §112, first paragraph, and thus, withdrawal of the rejection is respectfully requested.

Claim Rejections– 35 U.S.C. §112, second paragraph

The Examiner rejected claims 38-45, 50-62, 69-70, and 77-78 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner first stated that each of the rejected claims recites the term “wildtype” operator sequence. In the Examiner’s opinion, it is unclear what exactly is encompassed by this term. The Examiner stated “does the term refer only to operator sequences that are found in “nature” or can it encompass other sequences?” According to the Examiner, one of skill in the art, for example, would not normally consider the temperature-sensitive mutant cI857 as being a “wildtype” repressor, yet it appears from reading the instant application that the term “wildtype” operator sequence may be intended to mean any sequence that is mutated in the instant methods to produce an altered sequence with different thermostability characteristics.

In response, Applicants respectfully traverse this ground of the Examiner’s rejection. The term “wild type” as used in the present claims to refer to certain operator sequences is clear to one of ordinary skill in the art, particularly in light of the fact that the method relies on the

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recognition of a differential in thermostability between the mutated sequence and the wild type.

Moreover, Applicants point out that the wild type operator sequence of the bacteriophage lambda is described under accession number J02459; bacteriophage lambda, complete genome: Daniels, et al., Appendix II: Complete annotated lambda sequence (in) Hendrix et al., (EDS), Lambda II, 519-674, Cold Spring Harbor Laboratory, Cold Spring Harbor (1983). Corresponding sequences from lambdoid phages can be found by one of ordinary skill without undue effort. Accordingly, Applicants maintain that the claims are clear in their use of the term "wild-type" and thus respectfully request reconsideration and withdrawal of this aspect of the rejection.

The Examiner asserted that claim 38 is vague and indefinite in that the end result of the recited method does not recapitulate the preamble of the claim, making it unclear as to whether one had necessarily completed the method. The Examiner stated that the preamble states that the mutated operator sequence has a greater thermostability than the wildtype operator sequence with regard to binding to a repressor such that repression of a gene operatively linked to the mutated repressor until a temperature that is 3 to 10° C higher than the temperature at which the wildtype sequence is capable of repressing expression of an operatively linked gene. According to the Examiner, there is no positive action step, however, that necessarily relates back to this very specific functional limitation. The Examiner suggested amending the claim to include a positive action step that directly relates back to this limitation (e.g. where mutated operator sequences are selected that mediate repression of expression of the operatively linked gene at a temperature that is 3 to 10° C higher than the temperature at which the wildtype sequence is capable of repressing

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expression of the operatively linked gene).

The Examiner also asserted that claim 38 is vague and indefinite in that there is no clear and positive prior antecedent basis for the term "said DNA sequence" in line 4 of the claim. The Examiner pointed out for example, that OR, OL and wildtype operator sequences have been already recited in the claim and suggested amending the claim to clearly indicate that the term "said DNA sequence" refers to a mutated OR or OL sequence obtained from a lambdoid phage. Likewise, the Examiner asserted that claims 69-70 are vague and indefinite in that there is no clear and positive prior antecedent basis for the term "said DNA sequence" in line 10 of claim 69 or in line 11 of claim 70, respectively.

In response, without conceding the correctness of the Examiner's position, but to expedite allowance of the subject application, Applicants have amended claims 38, 69, and 70, to include a reference back to the preamble and to address the Examiner's concerns with respect to the recitation of "said DNA sequence". Applicants have also made minor changes to the claims to improve their clarity.

The Examiner stated that claim 50 is vague and indefinite in that it depends from a cancelled claim (i.e. claim 46).

In response, claim 50 has been amended to no longer depend from claim 46.

The Examiner asserted that claims 69-70 are vague and indefinite in that the recitation of the generic term "compared to a wildtype sequence" is unclear. The Examiner asked "to what

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‘wildtype’ sequence is the comparison to be made?”

In response, without conceding the correctness of the Examiner’s position, but to expedite allowance of the subject application, Applicants have amended the claims to address this concern. Applicants maintain that the claims are clear to one of ordinary skill in the art, particularly in light of the teachings in the specification.

The Examiner stated that claims 77-78 are vague and indefinite in that it is unclear how these claims further limit the claims from which they depend. According to the Examiner, the claims recite the limitation of further comprising “a gene for a first cI repressor.” In the Examiner’s view, there is no clear and positive prior antecedent basis for the term “a” gene encoding a “first” cI repressor. The Examiner asked “does the gene of claims 77-78 necessarily encode the ‘first’ cI repressor that can bind the OR or OL operator sequence of part (a) of the claim, or can it be some other ‘first cI repressor’?”

In response, without conceding the correctness of the Examiner’s position, but to expedite allowance of the subject application, Applicants have amended claims 77-78 for clarity by replacing “a” with “the” as appropriate.

Applicants believe that the claim amendments and remarks set forth herein fully overcome the rejections under 35 U.S.C. §112, second paragraph. Accordingly, Applicants respectfully request reconsideration and withdrawal of these rejections.

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Allowable subject matter

The Examiner has indicated that claim 49 is allowable. Applicants acknowledge and appreciate the allowance of this claim.

In view of the above remarks and amendments, Applicants believe that the Examiner's rejections set forth in the June 15, 2004 Office Action have been fully overcome and that the present application is in condition for allowance. The Examiner is invited to telephone the undersigned if it is deemed to expedite allowance of the application.

No fee is believed due in connection with the filing of this Amendment. If however, any fee is deemed necessary, authorization is hereby given to charge such fee, or credit any overpayment, to Deposit Account No. 02-2135.

Respectfully submitted,



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